

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>A61K 7/42, 7/44</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 99/33439</b> <b>(43) International Publication Date:</b> 8 July 1999 (08.07.99)
<b>(21) International Application Number:</b> PCT/US98/27433 <b>(22) International Filing Date:</b> 22 December 1998 (22.12.98)  <b>(30) Priority Data:</b> 08/998,238 24 December 1997 (24.12.97) US 09/113,815 10 July 1998 (10.07.98) US  <b>(71) Applicant (for all designated States except US):</b> SHAKLEE CORPORATION [US/US]; Shaklee Terraces, 444 Market Street, San Francisco, CA 94111 (US).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> GREENE, James, A. [US/US]; 991-6 Asilomar Terrace, Sunnyvale, CA 94086 (US). SIDDIQUI, Mukhtar [US/US]; 3172 Riviera Way, San Ramon, CA 94583 (US). ROBERTS, Richard, L. [US/US]; 1977 Kostka Lane, Germantown, TN 38139 (US).  <b>(74) Agent:</b> NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Winston, LLP, Suite 1600, One World Trade Center, 121 S.W. Salmon Street, Portland, OR 97204 (US).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> COMPOSITION WITH HIGH EFFICIENCY SKIN PROTECTION FROM DAMAGING EFFECTS OF ULTRAVIOLET LIGHT		
<b>(57) Abstract</b> <p>A topical antioxidant composition for the protection of skin from damage caused by ultraviolet radiation. The composition includes a first component (such as beta glucan or grape seed extract) that increases cellular viability of epidermal cells, and a second component that decreases the production of inflammatory mediators, such as prostaglandins, in those cells. In a particular embodiment, the composition includes beta glucan in combination with panthenol, grape seed extract, vitamin C and superoxide dismutase, which exhibit a synergistic effect in protecting the skin from the adverse effects of ultraviolet radiation. In another embodiment, the composition further includes Vitamin A and Vitamin E. In a further embodiment, the composition includes a combination of one or more antioxidants and sunscreen agents in an emulsion, such as water-in-oil (W/O) emulsion, which provides superior protection of the skin against the harmful effects of ultraviolet radiation. The antioxidant compositions are incorporated into sunscreen products, soap, moisturizing lotions, skin toners, and other skin care products.</p>		

## COMPOSITION WITH HIGH EFFICIENCY SKIN PROTECTION FROM DAMAGING EFFECTS OF ULTRAVIOLET LIGHT

### FIELD OF THE INVENTION

5           This invention concerns a topical antioxidant composition for the protection and treatment of human skin, particularly skin that is exposed to harmful ultraviolet radiation.

### BACKGROUND OF THE INVENTION

10           The ultraviolet (UV) wavelengths of sunlight can cause sunburn (erythema) and blistering (edema). Exposure to ultraviolet light can also cause the skin to feel dry and taut in moderate doses, and to peel if exposed to higher doses. These acute, or short term, effects are readily perceptible. However, there are also more subtle acute effects that are not as readily discernable, such as photo-  
15           immunosuppression, cross-linking of deoxyribonucleic acid (DNA), formation of sunburn cells, and loss of Langerhans cells. Even more serious long term effects can occur, such as skin cancer and premature aging of the skin.

          Sunscreen products are known to protect the skin from some of the harmful effects of ultraviolet light exposure. These products contain molecules that absorb  
20           the harmful wavelengths of ultraviolet light before they can reach the skin. The absorbed light is converted to heat and rapidly dissipated to the skin and environment, which allows these molecules to revert to a lower energy state, and subsequently absorb another photon of light. In this manner, sunscreen agents can absorb numerous photons of ultraviolet light in a relatively short period of time.  
25           By absorbing the harmful wavelengths of light, sunscreen products prevent many of the acute and chronic effects caused by ultraviolet light.

          However, sunscreen products are not perfect in their mode of action. No single sunscreen agent is capable of absorbing all of the harmful wavelengths striking the skin. Higher Sun Protection Factor (SPF) formulations address this  
30           problem by including a combination of sunscreen agents in the formulation. However, even when using a combination of sunscreen agents, these products do

Protection Factor is defined in accordance with the definitions in the Proposed Monograph. This same publication also describes the clinical testing procedure mandated for determining whether sunscreen products are waterproof, water resistant and sweatproof.

5           The labeled SPF values are generally recognized as being between 2 and 50. This is not meant to imply that SPF values greater than 50 are unachievable given the previous formulation technology. However, the amounts of sunscreen agents needed to achieve such high SPF values are usually cost prohibitive given current formulation technologies. The concentration of sunscreen agents needed  
10 to satisfy a "waterproof" designation are particularly high, because some of the agents are washed away in the test that measures SPF for a waterproof composition.

          A waterproof product is one that exhibits its labeled SPF value after 80 minutes of exposure to water under conditions that simulate swimming for that  
15 period of time. A water resistant product is similarly defined, except that it must withstand 40 minutes of water exposure. Although there is a separate test for the sweatproof claim, the Proposed Monograph allows products that pass the waterproof or water resistant claim to also carry the sweatproof claim.

          The most common sunscreen products sold in today's market are oil-in-  
20 water emulsions incorporating stearic acid neutralized with triethanolamine. The SPF values of such emulsions range from 2 to 50, and they commonly include ethylhexyl methoxycinnamate as the sunscreen agent. As the SPF of these formulations increases, they commonly contain ethylhexyl salicylate, homosalate, octocrylene and/or oxybenzone in addition to the ethylhexyl methoxycinnamate  
25 mentioned above. Alternatively, padimate O can be used in place of the ethylhexyl methoxycinnamate or the salicylates mentioned above. Dioxybenzone, avobenzone or menthyl anthranilate can be used in place of oxybenzone. If the product does not claim to be substantive to the skin (*i.e.*, waterproof or water resistant), trolamine salicylate or DEA methoxycinnamate can be used in place of  
30 (or in combination with) the ethylhexyl methoxycinnamate, ethylhexyl salicylate or homosalate. Additionally, sulisobenzene may be used in such non-substantive

mediators produced by free radicals. Compositions that incorporate Vitamins A or E, or their derivatives, in sunscreen compositions, are shown in U.S. Patent Nos. 4,454,112; 5,532,805; and 5,378,461. The use of Vitamin C in combination with Vitamins A, E, B and other agents in a skin protectant composition, is  
5 described in U.S. Patent No. 4,938,960. An antioxidant preparation that is said to protect the skin against harmful ultraviolet radiation is disclosed in U.S. Patent No. 5,607,921, and contains Vitamin C, in combination with Vitamins A and E, and monosaccharide or amide precursors. Sunscreen compositions containing panthenol and other agents are disclosed in U.S. Patent Nos. RE 33,845;  
10 5,505,935; 5,445,823; and 5,573,754. The antioxidant effect of superoxide dismutase when externally applied to the skin to protect against the effects of ultraviolet radiation is also described in U.S. Patent No. 5,601,806.

In spite of advances in recent years in the protection of skin from harmful ultraviolet radiation, the epidemic of skin cancer and skin damage from the effects  
15 of this radiation has continued unabated. The loss of portions of the ozone layer from environmental pollution is believed to have contributed to an increase in ambient ultraviolet radiation that reaches exposed skin. Many skin protection preparations that could prevent sun damage have an unacceptable odor or texture that discourages their more frequent use, and many of the available skin  
20 protectants do not sufficiently protect the skin from these many mechanisms of injury. Hence there is a significant public health need for commercially acceptable or improved preparations that can be topically applied to human and animal skin, to offset the harmful effects of ultraviolet radiation.

25

## SUMMARY OF THE INVENTION

The present invention provides a therapeutic or cosmetic composition containing new antioxidants, or agents that reduce sun induced skin damage and inflammation by aborting the production of prostaglandins in the skin. The composition has a superior therapeutic or cosmetic effect. Certain embodiments  
30 provide more protection from the adverse effects of ultraviolet light, without

group consisting of one or more of panthenol, grape seed extract, Vitamin C, superoxide dismutase, Vitamin A or Vitamin E in a sufficient amount to reduce production of PGE<sub>2</sub>, or increase cellular viability, in the skin when applied topically. The Vitamin C may be in the form of magnesium ascorbyl phosphate, while the Vitamin A may be in the form of Vitamin A palmitate, and the Vitamin E may be in the form of Vitamin E acetate.

The invention also takes advantage of the surprising finding that a mixture of an antioxidant and a sunscreen in an emulsion, such as a water-in-oil (W/O) emulsion, exhibits unexpectedly superior protection of the skin against the detrimental effects caused by exposure to ultraviolet radiation. Another embodiment of the antioxidant composition is therefore a composition which comprises (or consists essentially of) the antioxidant, a sunscreen, and a sufficient amount of a non-volatile emulsifier (such as an organopolysiloxane, for example an alkylpolysiloxane, such as an alkyl dimethicone emulsifier, including a polysiloxane polyalkyl polyether copolymer) that enhances a sun protection factor (SPF) of the composition. The composition may comprise, for example, a low level of sunscreen agent (or agents) in combination with a mixture of antioxidants in a water-in-oil organopolysiloxane and polyglycerol fatty acid ester emulsion.

In particular embodiments, the sunscreen includes one or more agents selected from the group of ethylhexyl methoxycinnamate, DEA methoxycinnamate, padimate O, ethylhexyl salicylate, homosalate, TEA salicylate, oxybenzone, dioxybenzone, sulisobenzene, avobenzone, octocrylene, titanium dioxide, zinc oxide or menthyl anthranilate. In other embodiments, the sunscreen includes at least one UVA sunscreen agent selected from the group of oxybenzone, dioxybenzone, sulisobenzene, avobenzone or zinc oxide, and at least one UVB sunscreen agent, selected from the group of ethylhexyl methoxycinnamate, DEA methoxycinnamate, padimate O, ethylhexyl salicylate, homosalate, TEA salicylate, octocrylene or titanium dioxide. In other specific embodiments, the sunscreen comprises at least oxybenzone and at least one of ethylhexyl methoxycinnamate and octyl salicylate. The antioxidant in the composition may include a mixture of one or more of the individual antioxidants described above.

any other skin treatment composition. The composition may also be used in methods of protecting skin against the harmful effects of ultraviolet radiation, by applying topically to the skin an amount of the composition effective to reduce the production of PGE<sub>2</sub> in the skin, or improve cellular viability. The composition  
5 may be applied before or after exposure to the sun, but is preferably applied prior to sun exposure, for example immediately before sun exposure.

The foregoing and other objects, features, and advantages of the invention will become more apparent from the following detailed description of several embodiments.

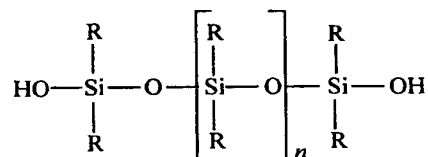
10

### DETAILED DESCRIPTION

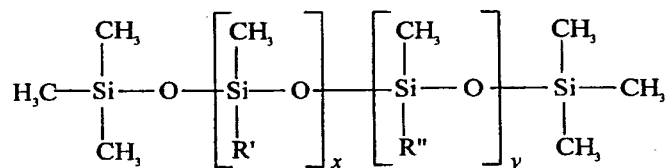
The combination of antioxidants in the present composition provides unexpectedly superior protection against the damaging effects of ultraviolet light exposure to that provided by the individual antioxidants. Furthermore, the present  
15 invention takes advantage of the surprising finding that a mixture of one or more of the antioxidants and sunscreen agents synergistically combine in a water-in-oil emulsion to provide unexpectedly superior protection to the skin against the harmful effects of ultraviolet radiation.

In some of the embodiments disclosed in the examples below, it is shown  
20 that a mixture of antioxidants exhibits more antioxidant activity than any of the individual antioxidant materials tested alone. In particular embodiments, it is also shown that this synergistic combination of antioxidants may be incorporated into a water-in-oil emulsion formulation that exhibits SPF values which far exceed SPF values that would be expected given the low concentration of sunscreen agents  
25 present in the formulation. The particular combination of antioxidants, and the low level of sunscreen agents in this water-in-oil emulsion system, are unexpectedly synergistic as measured by SPF values.

The sunscreen agents employed in the formulations are the same combinations used in some traditional formulations, such as ethylhexyl  
30 methoxycinnamate and oxybenzone. However, the levels of these sunscreen agents are significantly lower than those of more traditional oil-in-water sun care



In particular embodiments, the emulsifier is a non-volatile silicone oil, for example a polysiloxane polyalkyl polyether copolymer, also known as copolyols, having a molecular weight from 10,000 to 50,000, which are disclosed for  
 5 example in U.S. patent No. 5,746,945, which is incorporated by reference, and



include:

wherein the groups R' are each chosen from -H and C<sub>1-18</sub> alkyl, and R'' is -  
 [CH<sub>2</sub>CH<sub>2</sub>O]<sub>a</sub>[CH<sub>2</sub>(CH<sub>2</sub>)CHO]<sub>b</sub>H, in which a is 9 to 115, b is 0 to 50, x is 133 to  
 10 673, and y is 0.25 to 25. In particular embodiments, a is 14, b is 13, x is 249 and  
 y is 1.25.

The emulsifier can also include a dimethicone selected from alkyl- and alkoxy-dimethicone copolyols, such as those disclosed in U.S. Patent Application No. 5,659,523, which is incorporated by reference. A particularly preferred  
 15 copolyol is cetyl dimethicone copolyol, available from T.H. Goldschmidt as Abil EM-90, or Abil WE-09 (which also contains polyglyceryl-4-isostearate and hexyl laurate).

The term "aqueous" means that the composition is not substantially free of water. An emulsion is a dispersed system containing at least two immiscible  
 20 liquid phases. An emulsion in which water is the dispersed phase and oil is the dispersion medium is a "water-in-oil" emulsion. An "aqueous emulsion" refers to an emulsion that contains water as one of its phases.

weight percent) and available from Haarmann and Reimer (N.J.) under the tradename Sunarome UVA.

The compositions of the present invention preferably contain at least one UV-B type sunscreensing agent and at least one UV-A type sunscreensing agent.

5 The compositions of the present invention may also contain perfumes, preservatives, dyes, softeners, physical reflectors and other antioxidants, as well as any other class of materials whose presence may be cosmetically or otherwise desirable.

Other antioxidants include propyl, octyl and dodecyl esters of gallic acid, 10 butylated hydroxyanisole (usually as a mixture of ortho and meta isomers), butylated hydroxytoluene and nordihydroguaiaretic acid. Typical suitable preservatives include the lower alkyl esters of para-hydrobenzoates (parabens) especially, methyl paraben, ethyl paraben, propyl paraben, butyl paraben, isobutyl paraben and mixtures thereof, and benzoic acid. Typical suitable perfumes 15 include any oil soluble perfume or fragrance or mixture of perfumes or fragrances well known to those skilled in the art. Typical suitable physical reflectors include talc, kaolin, chalk, precipitated silica, zinc oxide, and titanium dioxide.

The compositions of the present invention may be in the form of a liquid, gel or semi-solid. The selection of ingredient type and amount is dictated by the 20 nature of the composition, i.e. gel or semi-solid, and is within the skill of cosmetic chemists. For example, larger amounts of wax are incorporated into the semi-solid compositions of the present invention than into the liquid ones.

The term "waterproofing effective amount of at least one waterproofing agent" means that if a waterproofing agent is used, the waterproofing agent(s) is 25 present in the composition at a concentration of at least 0.3 percent, and for example in the range 0.3 - 3 percent. Typical suitable waterproofing agents include copolymers derived from polymerization of octadecene-1 and maleic anhydride, for example using procedures such as those disclosed in U.S. Patent No. 3,860,700. A particular waterproofing agent is a copolymer commercially 30 available from Chevron Chemicals Co. under the tradename PA-18 polyanhydride



cocoa butter, olive oil, almond oil, macadamia nut oil, aloe extract, jojoba oil, safflower oil, corn oil, liquid lanolin, cottonseed oil, and peanut oil. Other suitable cosmetic emollients include Purcellin oil, perhydrosqualene, castor oil, polybutene, odorless mineral spirits, sweet almond oil, calophyllum oil, ricin oil, vitamin E acetate, mineral spirits, the oil of cereal germs, such as the oil of wheat germ, and esters such as isopropyl palmitate, isopropyl myristate, butyl myristate, hexadecyl stearate, decyl oleate, acetyl glycerides, the octanoates and benzoates of (C12-C15) alcohols, the octanoates and decanoates of alcohols and polyalcohols such as those of glycol and glycerol, ricin oleates of alcohols and poly alcohols, such as those of isopropyl adipate, hexyl laurate and octyl dodecanoate.

Cosmetic emollients which are solids or semi-solids at ambient temperatures may be used if admixed with one or more of the cosmetic emollients listed above, in amounts sufficient to provide liquid topical compositions. Such solid or semi-solid cosmetic emollients included hydrogenated lanolin, hydroxylated lanolin, acetylated lanolin, petrolatum, isopropyl lanolate, cetyl myristate, myristyl myristate, myristyl lactate, cetyl alcohol, isostearyl alcohol and isocetyl lanolate.

The following examples of the technology are meant to provide a better understanding of how to make and use the invention. Anyone skilled in the art of formulation will readily recognize other potential variants of the technology, which could be applied to formulations. Therefore, these examples are meant to demonstrate but not limit the scope of the patented technology. Definitions and suppliers of the ingredients used in the following illustrative examples may be found in the CTFA Cosmetic Ingredient Dictionary, published by the Cosmetic, Toiletry and Fragrance Association, Inc., Washington, D.C. 20005, Third Edition, 1982. All proportions are by percent weight, unless indicated otherwise.

### EXAMPLE 1

#### Cellular Viability Assay

This example describes how antioxidant activity was measured using a cellular viability assay. The antioxidant activity of individual and combinations of

ingredients, blends or controls. The total dose of ultraviolet light was 31.5 mJ/cm<sup>2</sup>. These cell cultures were then allowed to stand in normal growth media for 24 hours. After being allowed to grow for that period of time, the cell cultures were assayed for production of PGE<sub>2</sub> using the assay kit from PerSpective  
5 Diagnostics. The controls for this portion of the study were cell cultures exposed to the same dose of ultraviolet radiation but without added antioxidants (positive control). Three cell cultures were run for each antioxidant ingredient, blend or control sample tested. The results for these assays were then averaged.

The results of these tests from Examples 1 and 2 are shown in Tables 1 and  
10 2. The results shown in Table 1 indicate that all of the antioxidant agents and blends of these agents exhibit significant protective effect from ultraviolet light induced free radicals as measured by percent cellular viability. This activity must be as a result of the antioxidant effect because none of these agents exhibit any significant absorption in the solar ultraviolet wavelengths (290 to 400 nm) at the  
15 concentrations tested. Percent cellular viability after light exposure for blends A, B, and C is found in the data presented in Table 3. Although there are some statistically significant differences between individual antioxidant ingredients, the primary statistical differences are found between the blends of the agents and the individual agents composing the blends. For example, Blend B, composed of beta  
20 glucan, DL panthenol, grape seed extract, magnesium ascorbyl phosphate and superoxide dismutase, provides statistically superior protection to each of its individual components other than DL panthenol (data not shown). It might have been statistically superior to DL panthenol if the standard deviation of this antioxidant agent had been smaller. Blend A, composed of Vitamin E Acetate and  
25 Vitamin A palmitate, provides statistically superior protection when compared to its constituent ingredients at the 90% confidence level.

**TABLE 2**  
**Production of PGE<sub>2</sub> Resulting from UV Light Exposure**

5	from	Statistically Different	
		Average PGE <sub>2</sub> Produced	UV Irradiation
	Only		
	<u>Antioxidant Agent Tested</u>	<u>± Standard Deviation</u>	<u>(Confidence</u>
	<u>Level)<sup>1</sup></u>		
	Beta Glucan	14,900 ± 3630	No
	DL Panthenol	18,300 ± 5700	No
	Grape Seed Extract	13,300 ± 2640	No
	Magnesium Ascorbyl Phosphate <sup>2</sup>	15,100 ± 5390	No
	Superoxide Dismutase	22,900 ± 19,500	No
	Vitamin A Palmitate	17,400 ± 5720	No
	Vitamin E Acetate	26,000 ± 2750	No
	Blend A <sup>3</sup>	7140 ± 538	Yes (85%)
	Blend B <sup>4</sup>	861 ± 135	Yes (95%)
	UV Irradiation Only <sup>5</sup>	22,900 ± 11,000	-

<sup>1</sup> The level of statistical confidence is based upon hypothesis testing using a Student t test.

<sup>2</sup> This is a stabilized form of Vitamin C (Ascorbic Acid).

<sup>3</sup> Blend A is composed of Vitamin A Palmitate and Vitamin E Acetate.

<sup>4</sup> Blend B is composed of Beta Glucan, DL Panthenol, Grape Seed Extract, Magnesium Ascorbyl Phosphate and Superoxide Dismutase.

<sup>5</sup> This cell culture was exposed to UV light in the absence of added antioxidant materials.

Although many of these ingredients have been used in skin care products previously, the combinations are unique. The use of beta glucan to interfere with the production of an inflammatory mediator (such as PGE<sub>2</sub>), or to increase cellular viability following exposure to ultraviolet radiation, is also believed to be unique. Furthermore, the finding that these blends of antioxidant agents exhibit superior protection when mixed together is unexpected.

The combination of blends A and B, which is designated as Blend C in Table 3, was shown to provide statistically significant protection against the damaging effects of ultraviolet light using skin cell cultures. A comparison of this blend of antioxidants was found to be similar to the level of protection afforded by its oil and water soluble component blends. Based upon the results shown in Tables 1 and 2, there is evidence that Blend C provides more protection than its

**TABLE 5**  
**Statistical Comparison of Percent Cellular Viability**  
**Resulting from UV Light Exposure <sup>1</sup>**

<u>Antioxidant System</u>	<u>Blend B <sup>3</sup></u>	<u>Blend C <sup>4</sup></u>	<u>UV Irradiation Only <sup>5</sup></u>
Blend A <sup>2</sup>	NSD <sup>6</sup>	95 %	95 %
Blend B <sup>3</sup>	-	NSD	95 %
Blend C <sup>4</sup>	-	-	95 %

- <sup>1</sup> The values listed in this table are the statistical confidence level of difference based upon hypothesis testing using a Student t test.
- <sup>2</sup> Blend A is composed of Vitamin A Palmitate and Vitamin E acetate.
- <sup>3</sup> Blend B is composed of beta glucan, DL panthenol, grape seed extract, magnesium ascorbyl phosphate and superoxide dismutase.
- <sup>4</sup> Blend C is a mixture of Blends A and B.
- <sup>5</sup> This cell culture was exposed to UV light in the absence of added antioxidant materials.
- <sup>6</sup> NSD is an abbreviation for Not Statistically Different.

As shown in Tables 1 and 2, Blends A and B provide statistically significant protection from the damaging effects of ultraviolet light in both the Percent Cellular Viability and PGE<sub>2</sub> production assays. As further shown in Tables 3 and 4, Blend C (which is composed of the ingredients in both Blends A and B) also showed statistically significant protection in these same tests when compared to cell cultures without the addition of the antioxidants.

Regarding the results obtained specifically from the Percent Cellular Viability assay method as shown in Table 5, Blend A was found to provide statistically better protection than Blend C. Blends A and B were not found to provide statistically different levels of protection by this method nor were Blends B and C found to provide statistically different levels of protection from the damaging effects of ultraviolet light. In the previous test procedure (see Table 1) the same relationship was found for Blends A and B.

The results obtained specifically from the PGE<sub>2</sub> Production assay method are shown in Table 6, which illustrates that Blend B was found to provide statistically better protection than Blend A. This is the same result found in the previous test (Table 2) where Blend B showed substantially greater reduction of PGE<sub>2</sub> production than Blend A. As shown in Tables 4 and 6, Blend C was found

Although there are some statistical differences between the Blend C and blends of its oil or water soluble components, Blend C exhibits significant antioxidant activity in comparison to the individual ingredients tested previously.

Anyone skilled in the art of formulation will know how to readily  
5 incorporate these blends of antioxidant agents into suitable skin care and colored cosmetic products or into pharmaceutical products. Therefore, this information is intended to cover all possible combinations of these antioxidants in product formulations regardless of type or the market in which they are sold.

10

### EXAMPLES 3 - 10

#### Protective Skin Compositions

These examples describe formulations to demonstrate the typical use of the protective skin composition of the present invention in skin care and over the counter (OTC) pharmaceutical products. These formulations are listed only as  
15 examples of the types of compositions that could be used, and are not all encompassing of the possible uses of the technology in skin care and OTC pharmaceutical products. One skilled in the art of formulation will readily envision other possible uses for this technology, and the invention is not restricted the use of the formulations listed below. All ingredients of the formulations listed  
20 below are shown in percentage by weight (% w/w).

### EXAMPLE 3

#### Liquid Formulations

The following example is a general formula for liquid formulations of the  
25 composition.

	<u>Materials</u>	<u>General Use Range (Wt %)</u>
	Purified Water	19 - 98.7
	Surfactants	0.5 - 5
30	Witch Hazel Distillate	0.01 -20
	Humectant	0.5 - 5
	Fragrance	0.001 - 1
	Preservatives	0.2 - 3

	<u>Materials</u>	<u>General Use Range (Wt %)</u>
	Purified Water	0 - 98
	O/W Emulsifiers	1 - 12
	Humectants	0.5- 15
5	Fragrance	0.001 - 1
	Preservatives	0.1 - 3
	Sequestering Agent	0.01 - 0.5
	Emollients	0.5 - 30
	Thickeners	0.01 - 1
10	Vitamin A Palmitate	0.0005 - 0.5
	Vitamin E Acetate	0.05- 30
	Magnesium Ascorbyl Phosphate	0.0001-3
	Beta Glucan	0.005- 5
	Superoxide Dismutase	0.0001 - 1
15	Grape Seed Extract	0.00001- 1
	Panthenol	<u>0.005 - 5</u>
	<b>Total</b>	<b>100%</b>

20

**EXAMPLE 6****Skin Moisturizing Lotion**

The following example is an oil-in-water formulation developed as a moisturizing lotion for the skin.

	<u>Materials</u>	<u>Specific Use Concentration (Wt %)</u>
25	Purified Water	80
	O/W Emulsifiers	11
	Humectants	5
	Fragrance	0.05
30	Preservatives	2.7
	Sequestering Agent	0.1
	Emollients	12
	Thickeners	0.3
	Vitamin A Palmitate	0.05
35	Vitamin E Acetate	1
	Magnesium Ascorbyl Phosphate	0.25
	Beta Glucan	1
	Superoxide Dismutase	0.04
	Grape Seed Extract	0.005
40	Panthenol	<u>2</u>
	<b>Total</b>	<b>100%</b>

Superoxide Dismutase	0.004
Grape Seed Extract	0.0005
Panthenol	0.2
<b>Total</b>	<b>100%</b>

5

**EXAMPLES 9 and 10****Synthetic (Moisturizing) Soap Bar**

The following example is a general formulation for a moisturizing soap

10 bar.

	Example 9	Example 10
<u>Materials</u>	<u>General Use Range (Wt %)</u>	<u>Specific</u>
Purified Water	0 - 15	9.34
Detergents and Cleansing Agents	32 - 98	48.2
15 Buffering Agents	1 - 3	2.48
Humectants and Skin Conditioning Agents	0.5 - 5	13
Fragrance	0.001 - 1	0.24
Preservatives	0.01 - 2	0.09
Thickeners and Coloring Agents	0.01 - 30	25.67
20 Vitamin A Palmitate	0.0005 - 0.5	0.005
Vitamin E Acetate	0.05 - 30	0.5
Magnesium Ascorbyl Phosphate	0.0001 - 3	0.004
Beta Glucan	0.005 - 5	0.01
Superoxide Dismutase	0.0001 - 1	0.004
25 Grape Seed Extract	0.00001 - 1	0.195
Panthenol	0.005 - 5	0.195
<b>Total</b>	<b>100%</b>	<b>100%</b>

30

**EXAMPLES 11 and 12****Waterproof SPF 20 Sunscreens**

This example describes a waterproof SPF 20 formulation developed using a low level of sunscreens and the mixture of antioxidants in a water-in-oil emulsion.

Example 11 provides examples of general ranges of ingredients, while Example  
 35 12 provides a specific formulation. In these Examples, Phases A and B represent an oil soluble phase, while Phase C is a water soluble phase.

Phase C at 45 to 50°C. After completion of the addition, the batch was homogenized while maintaining a temperature of 45 to 50°C. After homogenization, the mixing was continued while beginning cooling to 30°C. Once at room temperature, the batch was packaged in appropriate containers.

- 5           The formulation exhibited a waterproof SPF of greater than 17.9 on five subjects. The formulation without the sunscreen agents, but with antioxidants, exhibited a waterproof SPF of only 2.8 on the same 5 subjects. The expected SPF for this combination of sunscreen agents alone would be less than 8, although the exact value was not determined. If the expected SPF of the sunscreen agents alone  
10 is added to the SPF resulting from the antioxidants, the total SPF (~ 10.8) is only 60% of that found for the resulting product.

### EXAMPLE 13

#### Waterproof SPF 30 sunscreen

- 15           This example describes a waterproof SPF 30 formulation developed using a low level of sunscreens and the mixture of antioxidants in a water-in-oil emulsion. All percentages are by weight. Phases A and B are oil soluble and Phase C is water soluble.

##### Phase A

20	Abil WE-09 (Goldschmidt)	8%
	Ethylhexyl Methoxycinnamate	7%
	Ethylhexyl Salicylate	3%
	Oxybenzone	2%
	C12-15 alkyl benzoate	6%
25	Octyl Palmitate	5%
	Cetyl Dimethicone	1%
	Castorwax MP-80	0.8%
	Microcrystalline Wax	1.2%

##### Phase B

30	Vitamin E Acetate	0.1%
	Vitamin A Palmitate	0.05%
	Cyclomethicone 345	1%

##### Phase C

35	Water	to 100%
	Magnesium Ascorbyl Phosphate	0.004%
	Sodium Chloride	0.3%
	Disodium EDTA	0.1%



Example 1 (increased epidermal cellular viability) or Example 2 (reduced PGE<sub>2</sub> production by epidermal cells). Ultraviolet radiation refers to electromagnetic radiation having a wavelength shorter than the wavelengths of visible light and longer than those of x-rays. Skin injury refers to cellular damage as measured by  
5 decreased cellular viability or increased PGE<sub>2</sub> production, or both. An antioxidant is a substance that opposes the effects of ROS, either by scavenging or reducing ROS, or interfering with the production of ROS.

Possible surfactants include polyoxyethylene sorbitan esters of fatty organic acids (such as laureate, palmitate, stearate, oleate and myristate) containing  
10 various molar concentrations of ethylene oxide (commonly listed as polysorbate 20, 21, 40, 60, 61, 65, 80, 81 and 85) as well as combinations of these ingredients.

Possible humectants include sugars (such as sorbitol, glucose, etc.), glycerin (and its polymers), glycols (such as propylene glycol, butylene glycol,  
15 and polyethylene glycols of various molecular weights), hyaluronic acid (and its salts), pyrrolidone carboxylic acid (and its salts) as well as combinations of these ingredients.

Possible preservatives include the parabens (such as the methyl, ethyl, propyl, isopropyl, butyl and isobutyl esters), imidazolidinyl urea, diazolidinyl  
20 urea, quaternium-15, phenylethyl alcohol, benzyl alcohol, phenoxyethanol, chlorphenesin, chlorhexidine digluconate as well as combinations of these ingredients.

Possible sequestering agents include the various salts of ethylenediamine tetraacetic acid (sodium, potassium, amine and amino acid salts).

25 Magnesium ascorbyl phosphate is a stabilized form of Vitamin C.

Stabilized forms of Vitamin A can be used in the preferred embodiment of the invention, such as the alcohol retinol or any of its esters. Other forms (such as Retin A) could also be used, but are less stable. Vitamin E is preferably used in its alcohol form (tocopherol), or any of its esters, or other stabilized forms.

30 Possible O/W surfactants include the salts of fatty acids (such as sodium, potassium, amine or amino acid salts of stearic, myristic, oleic, lauric or palmitic

Possible salts include sodium chloride, potassium chloride, lithium chloride and magnesium chloride or combinations of these ingredients.

Possible detergents and cleansing agents include the salts of cocyl isethionate, isostearoyl lactylate salts (such as the sodium and potassium salts),  
5 tallow and tallow salts (such as sodium, potassium and ammonium salts), salts of lauryl and laureth sulfates (such as sodium, potassium and ammonium salts), betaines and sultaines (such as cocamidopropyl betaine or sultaine) and salts of fatty acids (such as sodium or potassium laureate, myristate, palmitate, stearate, oleate, behenate, linoleate and ricinoleate) as well as combinations of these  
10 ingredients.

Possible buffering agents include all conventional buffering systems use in chemistry but especially lactic acid combined with a salt of lactic acid (such as sodium lactate) in appropriate ratios to maintain a given pH value.

Possible humectants and skin conditioning agents include the humectants  
15 listed above, salts of isostearoyl lactylate (such as sodium or potassium), quaternium compounds (such as stearamidopropyl dimethylamine) and oat by-products (such as oat flour) as well as combinations of these ingredients.

Possible thickeners and colorants include those thickeners listed above (see footnote 8) and colorants such as titanium dioxide, iron oxides, FD&C and D&C  
20 colorants, ultramarine blue, carmine, annatto, chlorophyll and other natural or artificial colorants as well as combinations of these ingredients.

In view of the many possible embodiments to which the principles of our invention may be applied, it should be recognized that the illustrated embodiments are only specific examples of the invention and should not be taken as a limitation  
25 on the scope of the invention. Rather, the scope of the invention is defined by the following claims. We therefore claim as our invention all that comes within the scope and spirit of these claims.

12. The method of claim 2, wherein the composition is provided in an emulsion that enhances an SPF of the composition.

13. The method of claim 3, wherein the composition is provided in an emulsion that enhances an SPF of the composition.

5 14. The method of claim 1, wherein the composition is provided in an emulsion that enhances an SPF of the composition.

15. The method of claim 1, wherein the emulsion is a polyorganosiloxane emulsion.

10 16. A topical composition for reducing skin damage induced by ultraviolet radiation, the composition comprising:

beta glucan in a sufficient amount to reduce the skin damage when applied topically; and

at least one other skin protectant that reduces the skin damage caused by ultraviolet light.

15 17. The topical composition of claim 16, wherein the other skin protectant is selected from the group consisting of one or more of panthenol, grape seed extract, Vitamin C and superoxide dismutase in a sufficient amount to reduce production of PGE<sub>2</sub>, or increase cellular viability, in the skin when applied topically.

20 18. The composition of claim 16, wherein the composition further comprises an antioxidant selected from the group consisting of one or both of Vitamin A and Vitamin E in a sufficient amount to reduce reactive oxygen species in the skin when applied topically.

25 19. The topical composition of claim 17, wherein the composition comprises about 0.005-5% beta glucan, 0.005-5% panthenol, 0.00001-1% grape seed extract, 0.0001-3% Vitamin C, and 0.0001-1% superoxide dismutase.

20. The topical composition of claim 17, wherein the composition comprises about 0.0005-0.5000% Vitamin A and 0.0500-30% Vitamin E.

30 21. The topical composition of claim 17, wherein the composition further comprises at least about 0.0005% Vitamin A, and at least 0.01% Vitamin E.

0.0001-3% Vitamin C; and  
0.0001-1% superoxide dismutase.

31. The composition of claim 28, comprising by weight at least  
about:

5           0.005% beta glucan;  
          0.005% panthenol;  
          0.00001% grape seed extract;  
          0.0001% Vitamin C; and  
          0.0001% superoxide dismutase.

10

32. The composition of claim 31, further comprising by weight at  
least about 0.0005% Vitamin A, and at least 0.05% Vitamin E.

33. The composition of claim 32, further comprising by weight  
about:

15           0.0005-0.5000% Vitamin A; and  
          0.0100-30% Vitamin E.

34. The composition of claim 16, in an aqueous or non-aqueous  
solution, suspension, a water-in-oil or oil-in-water emulsion.

35. The composition of claim 16 in a skin toner composition, a  
20 moisturizing lotion, a sunscreen composition, a skin cleanser or other skin  
treatment composition.

36. A topical antioxidant composition comprising a first component  
that increases cellular viability of epidermal cells, and a second component that  
decreases the production of PGE<sub>2</sub>.

25           37. A composition comprising:  
          an antioxidant that includes lipid soluble and water soluble  
          components;  
          a sunscreen; and  
          an emulsifier to emulsify a sufficient amount of the  
30 antioxidant and the sunscreen to provide a sun-protective composition.

46. The composition of claim 37, wherein the composition is at least 50% water, and the emulsifier includes 1-12% of an emulsification system that includes cetyl dimethicone copolyol, and the sunscreen agent and antioxidant are present in an amount sufficient to maintain the SPF of the composition at a value greater than about 15.

47. The composition of claim 37, wherein the sum of the SPF values of the antioxidant and sunscreen components tested separately is no more than about 70% of the SPF value of the sunscreen components tested together.

48. A method of improving an SPF value of a formulation for protecting skin from harmful effects of ultraviolet radiation, comprising combining one or more lipid soluble antioxidants with one or more water soluble antioxidants and one or more sunscreen agents, in the presence of an organopolysiloxane emulsifier, the formulation having the antioxidants, sunscreen agents and emulsifier present in an amount sufficient to enhance the SPF value of the formulation to greater than the sum of the SPF value of the antioxidants and sunscreen agents apart.

49. An ultraviolet radiation protective composition, comprising about 0.0002-4% of a lipid soluble sunscreen component that includes Vitamin A and Vitamin C; about 0.004-5% of a water soluble sunscreen component that includes Vitamin C, beta glucan, grape seed extract, and superoxide dismutase; an emulsifier; and a sunscreen component that contains less than about 12% of a non-particulate sunscreen agent that is substantially free of metal oxides.

50. The composition of claim 49, wherein the emulsifier comprises a polyalkylsiloxane.

51. The composition of claim 49, wherein the emulsifier further comprises a fatty alcohol.

52. The composition of claim 49, wherein the emulsifier comprises polyglyceryl-4-isostearate, cetyl dimethicone copolyol, and hexyl laurate.

53. A composition comprising about:

Primary emulsifier	1	-	9%
Ethylhexyl Methoxycinnamate	0.1	-	7.5%

	Ethylhexyl Methoxycinnamate	7%
	Ethylhexyl Salicylate	3%
	Oxybenzone	2%
	C12-15 alkyl benzoate	6%
5	Octyl Palmitate	5%
	Cetyl Dimethicone	1%
	Castorwax MP-80	0.8%
	Microcrystalline Wax	1.2%
	Vitamin E Acetate	0.1%
10	Vitamin A Palmitate	0.05%
	Cyclomethicone	1%
	Water	to 100%
	Magnesium Ascorbyl Phosphate	0.004%
	Sodium Chloride	0.3%
15	Disodium EDTA	0.1%
	Beta Glucan (Camamino)	0.1%
	Grape Seed Extract	0.5%
	Superoxide Dismutase	0.004%
	Fragrance and Preservatives	<u>q.s.</u>
20	<b>Total</b>	<b>100%</b>

wherein the primary emulsifier further comprises polyglyceryl-4-isostearate and hexyl laurate.

55. The composition of claim 53 wherein the primary emulsifier comprises polyglyceryl-4- isostearate, cetyl dimethicone copolyol and hexyl laurate.

56. A composition comprising about:

(a)

		<u>Percent by weight</u>
30	Purified Water	19 - 98.7
	Surfactants	0.5 - 5
	Witch Hazel Distillate	0.01 - 20
	Humectant	0.5 - 5
	Fragrance	0.001 - 1
35	Preservatives	0.2 - 3
	Sequestering Agent	0.01 - 0.5
	Menthol	0.005- 1
	Vitamin A Palmitate	0.0005 - 0.5
	Vitamin E Acetate	0.05 - 30
40	Magnesium Ascorbyl Phosphate	0.0001 - 3
	Beta Glucan	0.005 - 5
	Superoxide Dismutase	0.0001 - 1

- 43 -

		<u>Percent by weight</u>
	Purified Water	0 - 15
	Detergents and Cleansing Agents	32 - 98
	Buffering Agents	1 - 3
5	Humectants and Skin Conditioning Agents	0.5 - 5
	Fragrance	0.001 - 1
	Preservatives	0.01 - 2
	Thickeners and Coloring Agents	0.01 - 30
	Vitamin A Palmitate	0.0005 - 0.5
10	Vitamin E Acetate	0.01 - 30
	Magnesium Ascorbyl Phosphate	0.0001 - 3
	Beta Glucan	0.005 - 5
	Superoxide Dismutase	0.0001 - 1
	Grape Seed Extract	0.001 - 1
15	Panthenol	0.005 - 5
	<b>Total</b>	<b>100%</b>

or (e)

		<u>Percent by Weight</u>
20	Purified Water	9.34
	Detergents and Cleansing Agents	48.2
	Buffering Agents	2.48
	Humectants and Skin Conditioning Agents	13
	Fragrance	0.24
25	Preservatives	0.09
	Thickeners and Colorants	25.66
	Vitamin A Palmitate	0.005
	Vitamin E Acetate	0.49
	Magnesium Ascorbyl Phosphate	0.004
30	Beta Glucan	0.01
	Superoxide Dismutase	0.004
	Grape Seed Extract	0.195
	Panthenol	0.195
	<b>Total</b>	<b>100%</b>
35		

or (f)

		<u>Percent by weight</u>
	Purified Water	80
40	O/W Emulsifiers	11
	Humectants	5
	Fragrance	0.05
	Preservatives	2.7
	Sequestering Agent	0.1
45	Emollients	12

Panthenol	<u>0.2</u>
Total	100%

58. Any of the compositions of claim 56, further comprising a  
5 suncreen agent, and apolyorganosiloxane water-in-oil emulsion that increases an  
SPF of the composition.



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/27433

## A. CLASSIFICATION OF SUBJECT MATTER: US CL :

424/59, 60  
514/ 772, 772.3, 772.4, 844, 847, 937, 938

## B. FIELDS SEARCHED Minimum documentation searched Classification System: U.S.

424/59, 60  
514/ 772, 772.3, 772.4, 844, 847, 937, 938

